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EXAMINER	
LIU, SUE XU	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/502,510	EL-GEWELY, MOHAMED RAAFAT	
	Examiner	Art Unit	
	SUE LIU	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41-45,48-51 and 54-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *41-45,48-51 and 54-63* is/are rejected.

7)☒ Claim(s) *48 and 54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/23/10 has been entered.

Non-compliant Claim Amendment

2. The instant claims 52 and 53 are not provided with the proper claim status identifier. The said claims 52 and 53 should be "Canceled" as indicated by the deleted claim text. Appropriate correction is requested.

Claim Status

3. Claims 1-40, 46, 47, 52 and 53 have been cancelled as filed on 7/23/10.

Claims 56-63 have been added as filed on 7/23/10.

Claims 41-45, 48-51 and 54-63 are currently pending.

Claims 41-45, 48-51 and 54-63 are being examined in this application.

Election/Restrictions

4. Applicant's election without traverse of Group 3 (claims 38-51) in the reply filed on 5/19/2008 is as previously acknowledged. The newly added claims 56-63 are grouped with the Group 3 invention.

Priority

5. This application is filed under 35 U.S.C 371 of PCT/GB03/00291 (filed on 1/23/2003).

Claim Objection(s) / Rejection(s) Withdrawn

6. In light of applicants' amendments to the claims, the following claim rejection(s)/objection(s) as set forth in the previous office action is(are) withdrawn:

A.) The previous objection over claim 38 has been withdrawn due to cancellation of the said claim 38.

B.) Claims **38**, **41**, **42**, **45**, **48-51**, **54** and **55** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Shibata** et al (EP 0989136; 3/29/2000; cited in IDS), **Noaln** et al (WO 97/27212; 7/31/1997; cited in IDS), **Daniels** et al., (J. Mol. Biol. Vol. 243: 639-652; 1994), and if necessary, in view of **Tenson** et al. (J Biol. Chem. Vol.272(28): 17425-17430; 1997; cited in IDS).

C.) Claims **38**, **41**, **42**, **45**, **48-51**, **54** and **55** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Shibata** et al (EP 0989136; 3/29/2000; cited in IDS), **Noaln** et al (WO 97/27212; 7/31/1997; cited in IDS), **Daniels** et al., (J. Mol. Biol. Vol. 243: 639-652; 1994), and **Tenson** et al. (J Biol. Chem. Vol.272(28): 17425-17430; 1997; cited in IDS), as applied to

claims 38, 41, 45, 48-51, 54 and 55 above, and further in view of **Thornborrow** et al (JBC. Vol.274(47): 33747-33756; 1999; cited in IDS).

D.) Claims **38**, **41-45**, **48-51**, **54** and **55** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Shibata** et al (EP 0989136; 3/29/2000; cited in IDS), **Noaln** et al (WO 97/27212; 7/31/1997; cited in IDS), **Daniels** et al., (J. Mol. Biol. Vol. 243: 639-652; 1994), **Tenson** et al. (J Biol. Chem. Vol.272(28): 17425-17430; 1997; cited in IDS), and **Thornborrow** et al (JBC. Vol.274(47): 33747-33756; 1999; cited in IDS), as applied to claims 38, 41, 42, 45, 48-51, 54 and 55 above, and further in view of **Skarnes** (US 5,767,336; 6/16/1998; cited previously).

Claim Objection(s) / Rejection(s) Maintained

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 41-45, 48-51, and 54-63 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 28-49 of copending Application No. 10/493,582 (PGPUB 20070128657; hereinafter referred to as the '582 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the '582 application read on the instant claimed method. The previous rejection over claims 41-45, 48-51, 54 and 55 is maintained for the reasons of record as set forth in the previous Office action as well as for the reasons below. The rejection over claims 56-63 is necessitated by applicant's amendment to the claims.

The '582 application claims a method of screening a library of peptides using reporter system as recited in claim 1, which reads on the method of the instant claim 54 or 55.

The '582 application also claims various components of the reporter system, the target protein, the size of the library, etc., (as recited in claims 28-39), which reads on the instant claimed reporter system, target protein, etc., as recited in the instant claims 41-45, 48, 56, etc.

The '582 application also claims the screening assay is using p53 as the target binding proteins (e.g. claim 31), which reads on the p53 of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Discussion and Answer to Argument

9. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants has filed a terminal disclaimer over the '582 application. (Reply, p.5).

However, the terminal disclaimer was not approved by the Office due to the reason of "The Attorney did not sign the TD."

New Claim Objection(s) / Rejection(s)

Claim Objections

10. Claim 54 is objected to because of the following informalities: The term "the" in line 2 of step (a) of claim 54 after the phrase the wild type" should be deleted. Appropriate correction is required.

11. Claim 48 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Shibata

13. Claims **55**, **56**, **60** and **63** are rejected under 35 U.S.C. 102(**b**) as anticipated by (EP 0989136; 3/29/2000; cited in IDS).

The instant claims recite "a method of identifying a peptide of 2 to 8 amino acids in length having the ability to restore the wild type the function of p53 in an intra-cellular environment, the method comprising:

(a) introducing a library comprising peptides of 2 to 8 amino acids in length into host cells having a reporter system that allows for the identification of those cells in which the wild type function of p53 has been restored; and

(b) identifying a cell in which the wild type function of p53 has been restored; and

(c) identifying the peptide in the cell of step (b)."

Shibata et al, throughout the publication, teach various methods of screening a library of peptides with a reporter gene assay system (e.g. Abstract; pp.19+).

For **claim 55**: *"(a) introducing a library comprising peptides... into host cells having a reporter system..."* The reference teaches cells comprising a reporter system (e.g. pp.19-20, bridging), which read on the host cells having a reporter system of the instant claims. The reference also teaches introducing "test compounds" (i.e. a library of peptides; p.3, lines 30+) into the host cells (e.g. p.20, lines 40+; Tables 3-4), which reads on the step of introducing the library into host cells as recited in the instant claims. The reference also teaches the peptides can have 7 amino acid residues. For example, the Shibata reference teaches the general formula of

the peptides can be of 17 amino acids in length (e.g. pp.3+, para [0008]), which have deletions of various number of amino acids (such as 10 amino acids in length) (e.g. p.5, [0011]) and rendering the peptides to be of 7 amino acids in length.

The reference also teaches measuring the activation of p53 (i.e. restoration/modification of p53 activity) through the reporter gene expression (e.g. pp.19+; [0095]), which reads on "restored" p53 function of the instant claims.

"(b) identifying those cells in which the function of p53..." The reference teaches measuring the activity of the reporter cells and identifying the compounds that activated the reporter activity (e.g. p.21, Table 4), which cells containing the test peptides are "identified" through the measure of their reporter gene activities. The reference also identified the sequences of the peptides that activated/modified p53 function (e.g. p.22, [0110]).

"(c) identifying the peptide in the cell...": The reference teaches the identity of the testing peptides as the amino acid sequences of the peptides are identified (e.g. pp.20+; pp.31+; Abstract).

For **claim 56**: The reference teaches the reporter system comprise a reporter gene (e.g. luciferase) and a "P53 responsive element" in the transcription regulatory region (e.g. pp.19-20), which the reporter gene construct reads on the reporter system.

For **claim 60**: The reference teaches transfecting the reporter plasmid into the host cells (e.g. [0104]+), which reads on the transfection step.

For **claim 63**: The reference teaches using human cells (e.g. p.20, lines 46+), which reads on the eukaryotic cells.

Anderson

14. Claims **48-51, 54, 55** and **61-63** are rejected under **35 U.S.C. 102(b)** as being anticipated by **Anderson** et al. (U.S. Patent 6,180,343; 1/30/2001).

For **claims 48-51, 54, 55** and **61-63:** Anderson et al. teach methods comprising (a) transforming human host cells derived from diseased cells which naturally produce a non-wild type p53 mutant with a library of nucleic acid constructs that express peptides consisting of MG(X)n wherein the peptides are 4-50 amino acids in length and have a library size of 10^6 or more, (b) culturing the transformed host cells (e.g. eukaryotic cells, col.20, ll 5+) under conditions suitable for intracellular expression of the peptides, (c) analyzing the host cell population to determine the effect of the peptides on a reporter system which includes a target protein, secretion signal, and/or transmembrane domain, and the ability of the peptide(s) to restore the wild-type function of the target protein is analyzed, and (d) identifying the peptide (please refer to the entire specification particularly the abstract; columns 2, 4-7, 9, 11-15, 19-28). The reference teaches screening the library of peptides that will "restore" the p53 function in various cells (e.g. col.27-28; ll 60+). Please note: while Anderson et al. focuses on fusion polypeptide libraries, Anderson et al. also teaches additional screening methods wherein GFP fusions are not utilized (see column 25 for example).

Escher

15. Claims **41, 42, 45, 48, 50, 51, 54-57, 60, 62**, and **63** are rejected under **35 U.S.C. 102(b)** as being anticipated by **Escher** et al. (WO99/067375; 12/29/1999).

For **claims 54** and **55**, Escher et al. teach methods of screening peptide libraries comprising (a) transforming a host cell population with a DNA library that encodes the peptide library, (b) culturing the host cells and allowing for expression of the peptide library, (c) analyzing the host cells to determine the effect of the peptide library on a reporter system, and (d) identifying the peptide that provides a positive response (please refer to the entire specification particularly the abstract; Figures 1-4; columns 3-12; Examples 1-5). Regarding the peptide library, Escher et al. teach that the peptide library is generated from a random oligonuclelotide library about 15 to about 60 nucleic acids in length (i.e. 3 to 20 amino acids; please refer to the entire specification particularly Example 3). In addition, Escher et al. teach target proteins and analysis of the ability of peptides to restore the function of the target protein (e.g. wherein restoration of the function of the target protein is due to the peptide inducing the production and/or activity of a target protein; please refer to the entire specification particularly columns 3-4

For **claims 41, 42, 45, 48, 51, 56, 57, 60**, and **63:** Escher et al. teach p53 nucleic acid binding protein as a target protein, reporter genes, reporter genes operably linked to a nucleic acid sequence that is a binding sequence for the target protein, and transfection of the host cells with the reporter gene (please refer to the entire specification particularly Figures 2-4; columns 3-8 and 11-12). Escher et al. teach a p21 promoter (please refer to the entire specification particularly Figures 2-3).

For **Claim 50** and **62:** The reference also teaches the peptide can have various sizes such as "millions") (e.g. Figure 4).

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Shibata, Noaln and Escher

17. Claims **41**, **42**, **45**, **48-51**, **54-57** and **60-63** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Shibata** et al (EP 0989136; 3/29/2000; cited in IDS), **Noaln** et al (WO 97/27212; 7/31/1997; cited in IDS), **Escher** et al (WO99/067375; 12/29/1999), and if necessary, in view of **Anderson** et al. (U.S. Patent 6,180,343; 1/30/2001), **Tenson** et al. (J Biol. Chem. Vol.272(28): 17425-17430; 1997; cited in IDS) and/or **Thornborrow** et al (JBC. Vol.274(47): 33747-33756; 1999; cited in IDS).

The instant claims recite "a method of identifying a peptide of 2 to 8 amino acids in length having the ability to restore the wild type the function of p53 in an intra-cellular environment, the method comprising:

(a) introducing a library comprising nucleic acid constructs encoding peptides of 2 to 8 amino acids in length into host cells having a reporter system that allows for the identification of those cells in which the wild type function of p53 has been restored; and

(b) identifying a cell in which the wild type function of p53 has been restored; and

(c) identifying the peptide in the cell of step (b)."

Shibata et al, throughout the publication, teach various methods of screening a library of peptides with a reporter gene assay system (e.g. Abstract; pp.19+).

For **claims 54** and **55**: *"(a) introducing a library (comprising nucleic acid constructs encoding) of peptides... into host cells having a reporter system..."* The reference teaches cells comprising a reporter system (e.g. pp.19-20, bridging), which read on the host cells having a reporter system of the instant claims. The reference also teaches introducing "test compounds" (i.e. a library of peptides; p.3, lines 30+) into the host cells (e.g. p.20, lines 40+; Tables 3-4), which reads on the step of introducing the library into host cells as recited in the instant claims. The reference also teaches measuring the activation of p53 (i.e. restoration/modification of p53 activity) through the reporter gene expression (e.g. pp.19+; [0095]), which reads on "restored" p53 function of the instant claims.

"(b) identifying those cells in which the function of p53..." The reference teaches measuring the activity of the reporter cells and identifying the compounds that activated the reporter activity (e.g. p.21, Table 4), which cells containing the test peptides are "identified" through the measure of their reporter gene activities. The reference also identified the sequences of the peptides that activated/modified p53 function (e.g. p.22, [0110]).

"(c) identifying the peptide in the cell...": The reference teaches the identity of the testing peptides as the amino acid sequences of the peptides are identified (e.g. pp.20+; pp.31+; Abstract).

For **claim 41**: The reference teaches the reporter system comprise a reporter gene (e.g. luciferase) and a "P53 responsive element" in the transcription regulatory region (e.g. pp.19-20), which the reporter gene construct reads on the reporter system.

For **claim 45**: The reference teaches transfecting the reporter plasmid into the host cells (e.g. [0104]+), which reads on the transfection step.

For **claim 51**: The reference teaches using human cells (e.g. p.20, lines 46+), which reads on the eukaryotic cells.

Shibata et al do not explicitly state the peptides of the library have lengths ranging from 2 to 8 amino acids long as recited in **clms 54** and **55**. The Shibata reference also does not explicitly teach the size of the peptide library recited in **clm 50**. The reference also does not explicitly teach the peptide library has the sequence of M-G/M/V-(X)n as recited in **clm 49**. The Shibata reference also does not explicitly teach the "introducing a library comprising nucleic acid constructs…" as recited in **clms 48** and **54**.

However, **Shibata** et al. throughout the publication, teaches the peptides can have 7 amino acid residues. For example, the Shibata reference teaches the general formula of the peptides can be of 17 amino acids in length (e.g. pp.3+, para **[0008]**), which have deletions of various number of amino acids (such as 10 amino acids in length) (e.g. p.5, [0011]).

Noaln et al., throughout the publication, teach making and using peptide libraries in target screening assays (e.g. Abstract).

For **claims 54** and **55**: The reference teaches the method steps of (a) introducing a molecular library (peptide libraries) into cells, (b) screening the cells, (c) isolate/identify cell

with altered phenotype, (d) isolate/identify the library members (e.g. p.3, lines 6+), which reads on the screening method steps of the instant claims. The reference also teaches peptides with various lengths such as 9 amino acid residues (e.g. p.22, lines 15+).

The reference also teaches the screening assay can be used to identify library members (peptides) that can "reactivate" or "compensate" (or "restoration of the normal phenotype" i.e. wild type function) for p53 activity, especially in tumor cells (e.g. p.37, lines 25+).

For **claims 48** and **54**: The reference teaches generating nucleic acid constructs encoding for the peptides and introducing the constructs into cells (e.g. p.23), which reads on DNA constructs as well as the method step of introducing DNA into cells.

For **claims 50** and **62**: The reference also teaches the size of the peptide library are various such as 10^7 peptides (e.g. p.20, lines 4+), which reads on the library size.

For **claim 49** and **61**: The reference also teaches using peptide library with conserved consensus amino acid residues such as the ones with M and G residues (e.g. p.7; p.8; p.22), which reads on the conserved sequence.

Escher et al., throughout the publication, similarly, teach screening peptide libraries using a p53 specific reporter system (having p21 promoter) with peptides having various number of amino acids (such as 5 amino acids) (e.g. Examples and Figures), as discussed supra.

And/or, **Thornborrow** et al. teach using reporter gene constructs with either p21 or BAX promoter region that contains p53 response elements (or p53 binding regions) (e.g. p.33748, left col., para 3), which the promoters read on the promoters recited in **clm 42**. The reference also teaches the p21 and BAX promoters are regulated by p53, and the regulation is important in

various cellular mechanisms (e.g. p.33747). Thus, there is a great need to understand the interaction between the promoters and p53.

A person of ordinary skill in the art would have been motivated at the time of the invention to use p21 or BAX promoter region in the reporter gene construct for assaying p53, because p21 and BAX are known to substrate for p53 as taught by both Shibata et al and Thornborrow et al. In addition, due to the need to understand the interaction between p53 and its regulatory elements for various important cellular functions, a person of ordinary skill in the art would have been motivated at the time of the invention to use p21 or BAX promoters. In addition, because the both references teaches using reporter gene construct with p53 responsive elements (such as various promoter regions) for testing p53, it would have been obvious to one skilled in the art to substitute one known p53 responsive element (SV40 early promoter region) for the other (p21 or BAX promoter region) to achieve the predictable result of detecting measuring/testing p53 activation/function in a reporter gene assay system.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since both of the cited references have demonstrated the success of using reporter gene assays with various elements.

Further, if necessary, **Anderson** et al., teach screening a library of nucleic acid constructs encoding for peptides consisting of MG(X)n sequences wherein the peptides are 4-50 amino acids in length and have a library size of 10^6 or more, (b) culturing the transformed host cells (e.g. eukaryotic cells, col.20, ll 5+), as discussed supra.

Or **Tenson** et al., throughout the publication, teach minigene expression libraries (i.e. peptide libraries) comprising transforming host cells with a library of nucleic acid constructs encoding peptides of various lengths and formula MX_n, MVX_n, MMX_n, or MGX_n and culturing the host cells to allow for expression of the peptide library (e.g. Abstract; Figures 2B, 3, 4; pp.17425+). The reference teaches peptides having lengths such as 3-6 amino acids (e.g. Abstract; Figures 2 and 3).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to screen a library of peptides having various lengths (such as less than 8 amino acids), a library with various sizes and a peptide library with various sequences as well as using a library of encoding nucleic acid constructs.

A person of ordinary skill in the art would have been motivated at the time of the invention to use a library of peptides of small lengths such as 3 to 6 amino acids, because Shibata, Anderson, Escher all teach the need to identify small peptides (having less than 8 amino acids in length) that can "restore" p53 activity/function in host cells. In addition, because all the cited references (such as Shibata, Anderson, Escher and Tenson) teach methods of using/screening peptide libraries having various lengths, it would have been obvious to one skilled in the art to substitute one type of peptides (e.g. peptides with longer lengths such as 15 amino acids) for the other (e.g. peptides with shorter lengths such as 3-6 amino acids) to achieve the predictable result of screening/using peptide libraries to identify peptides of interest based on the purpose of the experimental design.

A person of ordinary skill in the art would have been motivated at the time of the invention to use peptide library of various sizes, because peptide library of various sizes are

known and routine in the art as taught by Noaln et al. In addition, it would have been obvious to one of ordinary skill in the art to apply the standard technique of generating peptide library of large size (such as at least 500 different members) as taught by Noaln et al, to improve the peptide library diversity and screening efficiency for the predicable result of enabling standard peptide library screening assays.

A person of ordinary skill in the art would have been motivated at the time of the invention to screen peptide library generated with certain conserved consensus amino acid residues depending on the screening target, because using peptides with conserved amino acid residues for targeted screening are known and routine in the art as taught by Noaln et al. In addition, because both of the Shibata and the Noaln references teaches screening peptide libraries, it would have been obvious to one skilled in the art to substitute one type of peptide libraries (with one type of consensus sequence) for the other (e.g. sequences with M and G residues) to achieve the predictable result of screening peptide libraries in a reporter gene assay system.

A person of ordinary skill in the art would have been motivated at the time of the invention to use encoding nucleic acid constructs to introduce peptides into cells, because using nucleic acid constructs offer the advantages of providing in vivo expressed peptides inside the cells, and using nucleic acid constructs are known and routine in the art as taught by Noaln et al. and Tenson et al. In addition, it would have been obvious to one of ordinary skill in the art to apply the standard technique of using encoding nucleic acid constructs to produce peptides in cells as taught by Noaln et al. and Tenson et al., to improve the peptide library availability inside

host cells for the predicable result of enabling standard peptide library screening assays inside cells.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since all of the cited references have demonstrated the success of using reporter gene assays with various elements.

Shibata and Others

18. Claims **41-45, 48-51** and **54-63** are rejected under 35 U.S.C. 103(a) as being unpatentable over **Shibata** et al (EP 0989136; 3/29/2000; cited in IDS), **Noaln** et al (WO 97/27212; 7/31/1997; cited in IDS), **Escher** et al (WO99/067375; 12/29/1999), and if necessary, in view of **Anderson** et al. (U.S. Patent 6,180,343; 1/30/2001), **Tenson** et al. (J Biol. Chem. Vol.272(28): 17425-17430; 1997; cited in IDS), and/or **Thornborrow** et al (JBC. Vol.274(47): 33747-33756; 1999; cited in IDS), as applied to claims 41, 42, 45, 48-51, 54-57 and 60-63 above, and further in view of **Skarnes** (US 5,767,336; 6/16/1998; cited previously).

The combination of the Shibata, Noaln, Escher and (Anderson or Tenson) references teaches methods of screening for peptides that can modify or restore p53 activity in cell reporter assay system, as discussed supra.

The above rejection over Shibata, Noaln, Escher and (Anderson or Tenson) references under 35 USC 103(a) is herein incorporated by reference in its entirety.

The combination of Shibata, Noaln, Escher and (Anderson or Tenson) references does not explicitly teach the reporter gene product include a secretion signal peptide as recited in **clm 43**, and a transmembrane domain as recited in **clm 44**.

However, **Skarnes** et al. teach generating reporter gene construct having secretion signals and transmembrane domains (e.g. cols.3, lines 20+), which read on the signal peptide and transmembrane domain as recited in **clms 43** and **44**. The reference also teaches the need to generate reporter gene encoding for fusion proteins having secretion signal and transmembrane domains for studying secretary proteins (e.g. cols.1-2).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to generate reporter proteins with secretion signal and transmembrane domains.

A person of ordinary skill in the art would have been motivated at the time of the invention to generate fusion reporter proteins having secretion signals and transmembrane domain, because including secretion signals and transmembrane in fusion reporter proteins are known and routine in the art as taught by Skarnes. As the Skarnes reference teaches the advantages of including secretion signals and transmembrane domains so that secretary proteins can be conveniently studied (e.g. cols.1-2), a person ordinary skill in the art would have been motivated at the time of the invention to generate fusion reporter proteins having secretion signals and transmembrane domain. In addition, it would have been obvious to one of ordinary skill in the art to apply the standard technique of generating fusion reporter proteins having secretion signals and transmembrane domains, as taught by Skarnes, to improve the reporter protein assay for the predicable result of enabling standard reporter gene assay system.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since all of the cited references have demonstrated the success of using reporter gene assays with various elements.

Discussion and Answer to Argument

19. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicant's traversal over the previous rejections are moot in light of the new rejections. In addition, applicants are respectfully directed to the above new rejection for answer to relevant arguments.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joanne Hama can be reached at 571-272-2911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Sue Liu/
Primary Examiner, AU 1639